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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/099,738	03/15/2002	Christian A. Heid	4498C1	5560

22896 7590 07/29/2003

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EXAMINER	
TUNG, JOYCE	
ART UNIT	**PAPER NUMBER**
1637	6

DATE MAILED: 07/29/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)
10/099,738	Heid et al.
Examiner	**Art Unit**
Joyce Tung	1637

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *May 6, 2003*.

2a) ☒ This action is **FINAL.** 2b) ☐ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *1-31* is/are pending in the application.

4a) Of the above, claim(s) _____ is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *1-31* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

1. The amendment filed 5/06/2003 has been entered. Following the entry of the amendment, claims 1-31 are pending.

Rejections and/or objected from the previous office action are hereby withdrawn. The following rejections are either newly applied or reiterated. They constitute the complete set presently being applied to the instant application.

Claim Rejections - 35 USC § 102

2. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371© of this title before the invention thereof by the applicant for patent.

3. Claims 1-16, 23 and 26-31 are rejected under 35 U.S.C. 102(e) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Aoyagi et al. (5,952,202).

Aoyagi et al. disclose a method and kit for quantitating nucleic acid amplification of control DNA in the presence of, and concurrently with, nucleic acid amplification of known and unknown target DNA. The kit contains internal control polynucleotide with 50-500bp in length (See column 7, lines 24-31). The method may be used in conjunction with variety of nucleic acid amplification system required the use of a nucleic acid polymerase with exonuclease activity (See

column 7, lines 56-67). This teaching is inherent that the kit includes a forward primer or reverse primer. The invention provided self-quenching fluorescence probes (See column 8, lines 10-14). The reporter dye of the probes is separated from the quencher dye by at least 12 nucleotides, attached at the 5' terminus or 3' terminus of the probe and the quencher dye is attached at the 5' terminus or 3' terminus (See column 8, lines 57-62). The kits make the practice of the method more reproducible and easier to perform (See column 10, lines 65-67). The kit includes nucleotide 5'-triphosphates (See column 11, lines 3-10). The reporter dyes are 6-FAM, TET and HEX as recited in claim 12 (See column 9, lines 10-32) and are xanthene dye (See column 28, claims 10 as recited in claim 10) and the quencher is rhodamine dyes as recited in claim 13 (See column 9, lines 33-56). The system may be generalized to include a plurality of fluorescent reporters (See column 8, lines 42-46). The self-quenching probes should be about 20-30 nucleotides long (See column 15, lines 18-21). The method involves a forward and reverse primers (See column 15, lines 22-23). The kit is comprised of all compositions needed for the method (See column 17, lines 27-34). The kit can be dispensed in automated manner to locations in spatially-addressable a test holder and the locations can be wells, sites or surface arrays. The location density is 96 wells (See column 11, lines 34-47).

The kit reagent used in the method of detection C-myc mRNA by exonuclease assay is 45 ul dispensed into each of all 96 wells (See column 19, lines 47-48). This teaching anticipates that each well has a 1 to 500ul volume as recited in claim 31.

Aoyagi et al. do not disclose the kit which comprises an external control polynucleotide. However, the language "external control" is intended use. Although Aoyagi et al. disclose an internal control polynucleotide, the internal control polynucleotide of Aoyagi et al. is equivalent to the external control of polynucleotide as claimed, since they both are polynucleotide used as control polynucleotide in polymerase chain reaction.

One of ordinary skill in the art would have been motivated to construct the kit comprising an external control polynucleotide as claimed because as addressed by Aoyagi et al., kits make the practice of a method more reproducible and easier to perform (See column 10, lines 65-66). It would have been prima facie obvious to make the kit as claimed.

The response argues that Aoyagi et al. do not teach that the forward primer and the detectable probe are separated by 0 to 5 nucleotides when hybridized to the external control polynucleotide, or its complement. However, these limitations are intended use and do not contribute to the patentability of the claims. Thus, the rejection is maintained.

Claim Rejections - 35 USC § 103

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103© and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

5. Claims 24-25 are rejected under 35 U.S.C. 103(a) as being unpatentable over Aoyagi et al (5,952,202).

The teachings of Aoyagi et al. are set forth in section 3 above, Aoyagi et al. do not disclose that the kit has a second single-stranded external control. Nevertheless, Aoyagi et al. disclose that the system may be generalized to include a plurality of fluorescent reports to monitor the simultaneous amplification of several target nucleic acids in a single reaction. Thus, it would have been prima facie obvious for one of ordinary skill in the art to include one more control polynucleotide in the kit for easier performing the method.

Further, Aoyagi et al. disclose 500 uM of dATP, dCTP, dTTP and dGTP used in a PCR reaction (See column 19, lines 48-49).

One of ordinary skill in the art at the time of the instant invention would have been motivated to construct a kit containing the amount of primer or self-quenching probe as needed

because constructing the kit with an optimized concentration of the primers and the probes with a reasonable expectation of success was routine practice in the art at the time of the instant inventions. It would have been prima facie obvious to make the kit as claimed.

The response argues that Aoyagi et al. do not teach that the forward primer and the detectable probe are separated by 0 to 5 nucleotides when hybridized to the external control polynucleotide, or its complement. However, as discussed in section 3, these limitations are intended use and do not contribute to the patentability of the claims. Thus, the rejection is maintained.

6. Claims 18-21 are rejected under 35 U.S.C. 103(a) as being unpatentable over Aoyagi et al. (5,952,202) as applied to claims 1-16, 23 and 26-31 above, and further in view of Kutyavin et al. (5,801,155).

The teachings of Aoyagi et al. are set forth in section 3 above, Aoyagi et al. do not disclose a kit which has a minor groove binder labeled with a detectable probe.

Kutyavin et al. disclose a minor groove binding molecules which are covalently bound to oligonucleotide (See the abstract and column 1, lines 34-47). Kutyavin et al. also address the combination of the minor groove binding molecules and oligonucleotide for hybridization probe and related analytical and diagnostic (See column 1, lines 48-53). Therefore, it would have been prima facie obvious for one of ordinary skill in the art to construct a kit including a minor groove binding molecules as claimed.

The response argues that neither Aoyagi et al. nor Kutyavin, alone or in combination teach that the forward primer and the detectable probe are separated by 0 to 5 nucleotides when hybridized to the external control polynucleotide, or its complement. However, as discussed in section 3, these limitations are intended use and do not contribute to the patentability of the claims. Thus, the rejection is maintained.

7. Claim 17 is rejected under 35 U.S.C. 103(a) as being unpatentable over Aoyagi et al. (5,952,202) as applied to claims 1-16, 23 and 26-31 above, and further in view of Livak et al. (5,538,848).

The teachings of Aoyagi et al. are set forth in section 3 above, Aoyagi et al. do not disclose that said quencher is non-fluorescent.

Livak et al. disclose a method for monitoring the process of nucleic acid amplification. The method involves quencher molecules which may or may not be fluorescent, depending on the embodiment of the invention. Non-fluorescent quenchers are referred to as chromogenic molecules (See column 5, lines 55-58). There are a lot of guidance available in the literature selecting appropriate reporter-quencher pairs for particular probes (See column 5, lines 61 to column 6, lines 1-15). Therefor it would have been prima facie obvious for one of ordinary skill in the art to construct a kit including a quencher which is non-fluorescent as needed as claimed.

The response argues that neither Aoyagi et al. nor Livak et al., alone or in combination teach that the forward primer and the detectable probe are separated by 0 to 5 nucleotides when

hybridized to the external control polynucleotide, or its complement. However, as discussed in section 3, these limitations are intended use and do not contribute to the patentability of the claims. Thus, the rejection is maintained.

8. Claim 22 is rejected under 35 U.S.C. 103(a) as being unpatentable over Aoyagi et al. (5,952,202) as applied to claims 1-16, 23 and 26-31 above, and further in view of Williams et al. (6232,075).

The teachings of Aoyagi et al. are set forth in section 3 above, Aoyagi et al. do not disclose one or more nucleotide 5'- triphosphates comprises a fluorescent dye as claimed in claim 22.

Williams et al. disclose the method comprising detecting and identifying individual fluorogenic dNTP molecules as a polymerase incorporates them into a single DNA molecule (See column 11, lines 35-38). Williams et al. disclose that in single molecule detection, high quenching efficiency is advantageous as it reduces fluorescence background, thus permitting the use of higher nucleotide concentrations (See column 11, lines 59-61). Therefore, it would have been prima facie obvious for one of ordinary skill in the art at the time of the instant invention to include the nucleotide 5'- triphosphates comprising a fluorescent dye in the kit as claimed.

The response argues that neither Aoyagi et al. nor Williams, alone or in combination teach that the forward primer and the detectable probe are separated by 0 to 5 nucleotides when hybridized to the external control polynucleotide, or its complement. However, as discussed in

section 3, these limitations are intended use and do not contribute to the patentability of the claims. Thus, the rejection is maintained.

Summary

9. No claims are allowable.

10. Any inquiries concerning this communication or earlier communications from the examiner should be directed to Joyce Tung whose telephone number is (703) 305-7112. The examiner can normally be reached on Monday-Friday from 8:00 AM-4:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached at (703) 308-1119 on Monday-Friday from 10:00 AM-6:00 PM.

Any inquiries of a general nature or relating to the status of this application should be directed to the Chemical/Matrix receptionist whose telephone number is (703) 308-0196.

11. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Art Unit 1637 via the PTO Fax Center located in Crystal

Mall 1 using (703) 305-3014 or 308-4242. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989).

Joyce Tung
J.T
July 17, 2003

ETHAN WHISENANT
PRIMARY EXAMINER

12. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.